UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/915,580	07/27/2001	Shinya Uchida	0397-0431P	8191

2292 7590 08/04/2003

BIRCH STEWART KOLASCH & BIRCH
PO BOX 747
FALLS CHURCH, VA 22040-0747

EXAMINER	
COOK, LISA V	
ART UNIT	**PAPER NUMBER**
1641	4

DATE MAILED: 08/04/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/915,580	Applicant(s) UCHIDA ET AL.	
	Examiner Lisa V. Cook	Art Unit 1641	

-- Th MAILING DATE of this communication appears on th cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *27 May 2003* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-11* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-11* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Amendment Entry

1. Applicant's response to the office action mailed 24 February 2003 is acknowledged. Applicant request for reconsideration fled therein has been carefully considered.

2. Currently, claims 1-11 are pending and under consideration.

OBJECTIONS MAINTAINED

Priority

3. Receipt is acknowledged of papers submitted under 35 U.S.C. 119(a)-(d), which papers have been placed of record in the file. Application No. 2000-226270 filed in JAPAN 7/27/00.

Should applicant desire to obtain the benefit of foreign priority under 35 U.S.C. 119(a)-(d) prior to declaration of an interference, a translation of the foreign application should be submitted under 37 CFR 1.55 in reply to this action.

Applicants decline the Examiners invitation to incur the expense of providing an unnecessary certified English translation of the priority document at this time.

Information Disclosure Statement

4. The listing of references in the specification is not a proper information disclosure statement. For example see page 12. 37 CFR 1.98(b) requires a list of all patents, publications, or other information submitted for consideration by the Office, and MPEP § 609 A(1) states, "the list may not be incorporated into the specification but must be submitted in a separate paper." Therefore, unless the examiner-on form PTO-892 or the applicant-on form PTO-1449 have cited the references they have not been considered.

REJECTIONS MAINTAINED

Claim Rejections - 35 USC § 103

5. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negative by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

I. Claim 1 is rejected under 35 U.S.C. 103(a) as being unpatentable over Yamao et al. (US Patent #6,030,845) in view of JP 60047962 to Terumo Corp – Abstract Only.

Yamao et al. disclose an immunoassay method for lysed whole blood. Antibodies in the sample (whole blood) are subjected to agglutination reaction with insoluble carriers or an insoluble particle suspension reagent on to which the antibodies or antigens are immobilized. The agglutination mixture may be lysed with a low osmotic solution, a solution of saponins, freeze/thawing, or by ultrasonication. The resulting agglutination reaction mixture is analyzed for the change in absorbance or in its light scatter by irradiation. See abstract and column 2, lines 9-67.

Yamao et al. differ from the instant invention in not teaching agglutination before the introduction of an erythrocyte-lysing agent (hemolysis).

However, in patent JP 60047962 hemolyzing agents directed to erythrocyte lysing are employed. A whole blood sample is treated with polystyrene latex sensitized with human gamma globulin (to initiate agglutination) and the sensitized latex was mixed with 0.5% Bovine serum albumin and 0.4% saponin (hemolysing agent) to form a reagent for the detection of rheumatoid factor in whole blood. See abstract.

It would have been obvious to one of ordinary skill in the art at the time of the invention to agglutinate before utilizing the lysing agent as taught by Terumo Corp (JP60047962) in the method of Yamao et al. because Terumo Corp (JP60047962) taught that "hemolyzing agents cause hemolysis of erythrocytes which interfere with the agglutination reaction". See abstract. One of ordinary skill in the art at the time the invention was made would have been motivated to agglutinate prior to lysing to eliminate the interference exhibited when the process is reversed.

II. Claims 2 and 3 are rejected under 35 U.S.C. 103(a) as being unpatentable over Yamao et al (U.S.Patent #6,030,845) in view of JP 60047962 to Terumo Corp – Abstract Only and in further view of Bester et al. (Analytical Biochemistry, Vol. 223, No.2, pages 299-305, 1994).

Please see Yamao et al. in view of JP 60047962 to Terumo Corp are set forth above.

Yamao et al. in view of JP 60047962 to Terumo Corp differ from the instant invention in not specifically teaching the utility of an erythrocyte-lysing agent (such as sodium dodecyl sulfate) to lyse erythrocytes.

However Bester et al. teach methods of employing and optimizing lysing agents like sodium dodecyl sulfate (SDS). See abstract. Bester et al. further disclose that the use of SDS with fluorescent dyes could be optimized to quantify DNA in cell cultures. See page 299 2nd column 1st paragraph.

It would have been obvious to one of ordinary skill in the art at the time of the invention to employ SDS as a lysing agent to lyse cells as taught by Bester et al. in the method of Yamao et al. in view of JP 60047962 to Terumo Corp because Bester et al. taught that SDS was effective in cell dissolution. See page 299, 2nd column, 1st paragraph. One of ordinary skill in the art at the time the invention was made would have been motivated to incorporate the SDS in cellular analysis to therein take advantage of its known dissociation properties.

III. Claims 4-9 are rejected under 35 U.S.C. 103(a) as being unpatentable over Yamao et al. (U.S.Patent #6,030,845) in view of JP 60047962 to Terumo Corp – Abstract Only and further in view of Kosako (U.S.Patent #5,527,714) and Cohen et al. (U.S.Patent #4,851,329).

Please see Yamao et al. in view of JP 60047962 to Terumo Corp as set forth above.

Yamao et al. in view of JP 60047962 to Terumo Corp fail to particularly teach flow cytometry analysis, particle size, and particle to sample ratios.

However, Kosako disclose a method for determining particle size distributions with respect to an analyte via mediated particle agglutination. The method involves the utility of antigen/antibody reactions to concentrated sensitized insoluble carriers into non-aggregated and aggregated particles of known size.

The analyte is analyzed by an electronic analyzer to detect the quantity and size distribution of concentrated non-aggregated and aggregated insoluble carriers resulting from the antigen/antibody reaction, as well as spurious particles that may be present in the analyte. See column 1 line 65 through column 2 line 9. The calculation with respect to T and M as recited in claim 6 is taught by Kosako (5,527,714) column 4 lines 36-50.

Cohen et al. also disclose a method of determining the concentration of antibody and antigen molecules with high specificity, accuracy, and sensitivity. The process can be used to determine concentration of any substance capable of promoting or inhibiting an agglutination reaction. See abstract. The process is based on the relationship between cluster size of aggregated particles and the intensity of light scatter from the particles as they traverse a beam of focused light. Column 2 lines 62-67. The particle size range from 0.03 up to about 5-10 microns. Column 4, lines 24-26. In the example in column 7 the mixture of particle to sample was taught to be 1:11 (see column 7 lines 54-55).

It would have been obvious to one of ordinary skill in the art at the time of the invention to incorporate the flow analysis teachings of Kosako and Cohen et al. into the method of Yamao et al. in view of JP 60047962 to Terumo Corp because Kosako taught that his method detected small percentages of an analyte with improved sensitivity and decreased sample preparation time. Column 1 lines 30-34. The agglutination process further allowed for spurious particle elimination Column 2 lines 10-16. While, Cohen et al. taught that his method resulted in high intrinsic sensitivity and specificity of the agglutination reaction, improved light scatter detection, while identifying contaminants. Column 6 line 57 through column 7 line 25.

One of ordinary skill in the art at the time the invention was made would have been motivated to measure agglutination in flow cytometry particle analyses to more accurately measure the analyte with various particle parameters thus allowing for increased data sets for consideration and evaluation.

IV. Claims 10 is rejected under 35 U.S.C. 103(a) as being unpatentable over Yamao et al. (U.S.Patent #6,030,845) in view of JP 60047962 to Terumo Corp – Abstract Only and further in view of Holmes (U.S. Patent #4,830,969).

Please see Yamao et al. in view of JP 60047962 to Terumo Corp are set forth above.

Yamao et al. in view of JP 60047962 to Terumo Corp differ from the instant invention in not teaching the immune agglutination reaction temperature and time recited in claim 10.

However Holmes disclose a process for the separation of cellular materials. The cellular material is heated in a solution of lysing agent (including surfactants) to agglomerate water-soluble nitrogen containing compounds. See abstract.

In general the temperature is between about 60° and about 105°C., preferably between 80° and 105°C. The time is between about 10 seconds and about 3 minutes. Column 2, lines 54-63. Therein reading on the limitations of claim 10.

It would have been obvious to one of ordinary skill in the art at the time of the invention to utilize the temperature and time ranges taught by Holmes in the method of Yamao et al. in view of JP 60047962 to Terumo Corp because Holmes taught that this process (temp and time) allowed one to separate agglomeration resistant water soluble nitrogen containing cellular organic compounds like nucleic acids and peptides from other cellular materials. Column 2, lines 1-9.

Further the need for isolating plasmids and other nucleic acids has become critical due to the extremely rapid growth of microbiological analysis and genetic engineering. Column 1, lines 56-65.

One of ordinary skill in the art at the time the invention was made would have been motivated to utilize the process taught by Holmes because it was rapid, simple, and inexpensive. Column 1 lines 51-55.

Response to Arguments

6. Applicant contends that the cited references did not teach the instant invention because they taught hemolysis prior to agglutination. The instant invention is direct to a process wherein the sample is agglutinated first and subsequently hemolyzed. This argument was not found persuasive because Yamao et al. (6,030,845) teach that the utility of their hemolytic - lyses reagent has not effect on the agglutination reaction. (column 2 line 4). Accordingly the hemolytic step may be performed before or after the agglutination step. No more than routine skill is involved in adjusting the amount of a component of the claimed process to suit a particular starting material in order to achieve the result taught in the prior art. *Exparte Rasmussen* (POBA 1959) 123 USPQ 498.

Further both Yamao et al. and JP60047962 teach the simultaneous addition of both the agglutination reagents and lysing reagent. Although the instant disclosure teaches unexpected results over methods wherein blood samples are first hemolyzed followed by agglutination (Table 1 page 14), it does not show unexpected results when the reagents (agglutination and lyses) are added/conducted simultaneously.

Therefore it appears that the order of reagent addition or reaction steps are not critical. Absent evidence to the contrary the process of agglutinating prior to lysing is viewed as an obvious modification of the prior art method taught by Yamao et al. in view of JP60047962. It is also noted that a long list of cases have held that the mere use of different starting materials, whether novel or known, in a conventional process to produce the product one would expect there from does not render the process unobvious. *In re Surrey et al.* (CCPA 1963) 318 F2d 233, 138 USPQ 67; *In re Kanter* (CCPA 1968) 399 F2d 249, 158 USPQ 331; *In re Larsen* (CCPA 1961) 292 F2d 531, 130 USPQ 209.

With respect to the 103 rejections cited in items II through IV above, Applicant argues that the rejections must fail since the rejection of claim 1 is overcome. The argument was considered and not found persuasive. Therein the rejections are maintained.

7. For reasons aforementioned, no claims are allowed.

8. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Remarks

9. Prior art made of record and not relied upon is considered pertinent to the applicant's disclosure:

A. Lehnen (U.S. Patent #5,567,627) teach methods and reagents useful in the simultaneous and discrete analysis of multiple analytes.

B. Terstappen et al. (U.S. Patent #5,646,001) affinity-binding separation and release of one or more selected subset of biological entities from a mixed population thereof.

10. Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Group 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform to the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The Group 1641 Fax number is (703) 308-4242, which is able to receive transmissions 24 hours/day, 7 days/week.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Lisa V. Cook whose telephone number is (703) 305-0808. The examiner can normally be reached on Monday-Friday from 8:00 AM - 4:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long Le, can be reached on (703) 305-3399.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Lisa V. Cook
CM1-7B17
(703) 305-0808
7/30/03

LONG V. LE
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600
08/01/03